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Guidance for Industry

Effectiveness of Anthelmintics: Specific Recommendations for Poultry VICH GL21

DRAFT GUIDANCE

This guidance document is being distributed for comment purposed only

This draft guidance is intended to standardize and simplify methods used in the evaluation of new anthelmintics submitted for approval to the European Union, Japan, and the United States.

Comments and suggestions regarding the draft document should be submitted to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the Docket No. 00D-1629.

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EFFECTIVENESS OF ANTHELMINTICS:
SPECIFIC RECOMMENDATIONS FOR POULTRY

Recommended for Consultation
at Step 4 of the VICH Process
on 15 June 2000
by the VICH Steering Committee

THIS GUIDANCE HAS BEEN DEVELOPED BY THE APPROPRIATE VICH EXPERT WORKING GROUP AND IS SUBJECT TO CONSULTATION BY THE PARTIES, IN ACCORDANCE WITH THE VICH PROCESS. AT STEP 7 OF THE PROCESS THE FINAL DRAFT WILL BE RECOMMENDED FOR ADOPTION TO THE REGULATORY BODIES OF THE EUROPEAN UNION, JAPAN, AND USA.

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This draft guidance represents the agency's current thinking and does not create or confer any rights for or on any person, and does not operate to bind FDA or the public. An alternative method may be used as long as it satisfies the requirements of the applicable statutes and regulations.

Introduction

This guidance for poultry (chickens) was developed by the Working Group established by the Veterinary International Cooperation on Harmonisation (VICH), Anthelmintic Guidances. It should be read in conjunction with the VICH Effectiveness of Anthelmintic: General Recommendations Guidances (EAGR) which should be referred to for discussion of broad aspects for providing pivotal data to demonstrate product anthelmintic effectiveness. The present document is structured similarly to the EAGR with the aim of simplicity for readers comparing both documents.

The guidance for poultry is part of this EAGR and the aim is (1) to be more specific for certain specific issues for poultry not discussed in the EAGR; (2) to highlight differences with the EAGR on effectiveness data recommendations and (3) to give explanations for disparities with the EAGR.

A. General Elements

1 - The evaluation of effectiveness data

Only controlled tests based on parasite counts of adults/larvae are recommended both for the dose determination and dose confirmation studies, since critical tests generally are not considered to be reliable for poultry. They may be used in preliminary investigations. Egg counts with identification is the preferred method to evaluate the effectiveness in field studies. Adequate parasite infection should be defined in the protocol according to regional prevalence or historic and/or statistical data.

2 - Use of natural or induced infections

Dose determination studies generally should be conducted using induced infections with either laboratory or recent field isolates.

Dose confirmation studies could be conducted using naturally infected birds which can have superimposed induced infections of certain parasites that will not interfere with the resident intestinal population. This procedure will allow a wide range of parasites to be present in the experimental birds. Also induced infections in one of the studies is acceptable. Studies for larval stages should be conducted with induced infections only.

The history of the parasite cultures used in the induced infection studies should be included in the final report.

3 - Number of infective forms recommended for induced infections

Table 1 indicates the number of eggs/cysticercoids recommended to be used and will depend on the isolate that is used. The final number of eggs/cysticercoids used in the infection should be included in the final report.

Table 1 - Number of infective stages used to produce adequate infections in poultry for anthelmintic evaluation.

Parasites	Number of eggs/cysticercoids
Ascaridia galli	200 - 500
Capillaria obsignata	100 - 300
Heterakis gallinarum	200 - 300
Raillietina cesticillus	50 - 100
Syngamus trachea	200 - 600

Some factors to consider for induced infections in poultry:

a) Young birds should be used in the studies

b) Infection levels are critical for chickens, i.e. high numbers of infective forms do not generate heavy infections

c) Stress (e.g. poor diets) is not needed to generate helminth infections

d) Birds of both sexes should be evenly included in the study

e) Housing conditions should not allow accidental infections

4 - Recommendations for the calculation of effectiveness

4.1 Criteria to grant a claim

To be granted a claim, the following pivotal data should be included:

a) Two dose confirmation studies conducted with a minimum of 6 adequately infected birds in each of the non-medicated group and the treated group;

b) The differences in parasite counts between treated and control birds should be statistically significant ($p<0.05$);

c) Effectiveness should be 90% or higher calculated using transformed (geometric means) data of worm counts;

d) The infection of the birds in the study should be deemed adequate based on historical, parasitological, and/or statistical criteria.

4.2 Number of animals (dose determination and dose confirmation trials)

The minimum number of animals used per experimental group is a crucial point. Although the number of birds will depend on the possibility of processing the data according to an adequate statistical analysis, it has been recommended, to achieve harmonization, that the inclusion of at least 6 birds in each experimental group is a minimum.

4.3 Adequacy of infection

Concerning the minimum adequate number of helminths, the decision should be made when the final report is submitted based on statistical and historical data, literature review, or expert testimony. The range of chicken helminths (adults) considered adequate to grant a claim will vary according to the species. Generally the minimal mean number for *Ascaridia galli* is 20 adults. Lower counts may be expected with *Heterakis gallinarum*, *Capillaria obsignata* and *Raillietina cesticillus*. Necropsies should be conducted within 10 days of treatment.

4.4 Label claims

For adult claims, as a general rule, the treatment should not be administered earlier than 28 days after infection. It is recommended to include at least 6 sentinel birds for helminth characterization and quantification before treatment is initiated. For L4 claims, treatments should be given, as a general rule, 7 days after infection, except for *A. galli* and *H. gallinarum* which should be 16 days after infection.

5 - Treatment procedures

The method of administration (oral, parenteral, topical, slow release etc.), formulation and extent of activity of a product will influence the protocol design.

When the drug is to be administered in the water or in a premix, it should be done as much as possible following the labeling recommendations. Palatability/consumption studies may be recommended for medicated premixes. Samples of medicated water or feed should be collected to confirm drug concentration. The amount of medicated product provided to each animal should be recorded to ensure that the treatment satisfies the label recommendations.

6 - Bird selection, allocation, and handling

Test birds should be clinically healthy and representative of the age, sex, and class for which the claim of the test anthelmintic is to be made. In general, birds should be young and from a breed that is susceptible to helminth infections. Birds should be randomly assigned to each group. Blocking in replicates by weight, sex, age, and/or exposure to parasites may aid in reducing trial variance. Fecal egg counts are also recommended to allocate the experimental birds. Control birds should be of the same weight, age, breed, sex and history as the treated group. For induced infections, the use of helminth naive birds is recommended.

Animal housing, feeding and care should follow strict recommendations of welfare, including vaccination according to local practices. This information should be provided in the final report. A minimum 10-day acclimation period is recommended. Housing and feed/water should be adequate according to the geographical location. Birds should be monitored daily to determine adverse reactions.

B. Specific Evaluation Studies

1 - Dose determination studies

If the treatment requires extended administration, one or more studies are recommended to determine the minimum treatment period for effectiveness.

2 - Dose confirmation

No species specific recommendations.

3 - Field effectiveness studies

Due to commercial constraints the experimental unit in these studies invariably should be the shed/house. A shed/house can receive only one treatment, i.e. control or medicated.

Clinical observations, production parameters, and records of mortality should be maintained and compared to historical data of the commercial establishment. Slaughterhouse inspection reports should be included in the final report, when the number of test animals can not be confirmed.